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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/892,613	06/27/2001	Shawn Shui-on Leung	655	4914

7590 03/24/2006

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EXAMINER	
BLANCHARD, DAVID J	
ART UNIT	**PAPER NUMBER**
1643	

DATE MAILED: 03/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/892,613	LEUNG, SHAWN SHUI-ON	
	Examiner	Art Unit	
	David J. Blanchard	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 January 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *40-49* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *40-49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *27 June 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/27/01; 10/7/02;* 2/6/04
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be to directed to David Blanchard, Art Unit 1643.

2. Claims 1-39 and 50 are cancelled.

Claims 40 and 48 have been amended.

3. Claims 40-49 are pending and under examination.

4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

5. This Office Action contains New Grounds of Rejections.

Information Disclosure Statement

6. The information disclosure statement (IDS) submitted on 27 June 2001, 10 October 2002 and 06 February 2004 have been fully considered by the examiner. A signed copy of each IDS is included with this Office Action.

Rejections Withdrawn

7. The rejection of claim 50 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn in view of the cancellation of the claim.

8. The rejection of claims 40-44 and 46-50 under 35 U.S.C 112, second paragraph as being indefinite in the recitation "derived" and "whereas" in claim 40 is withdrawn in view of the amendments to the claims.

9. The rejection of claims 40-50 under 35 U.S.C. 103(a) as being unpatentable over Ohmoto et al (Molecular Immunology 32:407-416, 1995) in view of Queen et al (US Patent 5,693,762, issued 12/97, IDS filed 6/27/01) is withdrawn in view of applicant's arguments and the amendments to the claims which require FR1, FR2 and FR3 from different heavy and light immunoglobulin chains.

New Grounds of Objections/Rejections

10. The Examiner acknowledges Applicant's replacement Abstract filed 4/7/2003, however, the abstract of the disclosure is objected to because the abstract of the disclosure does not commence on a separate sheet in accordance with 37 CFR 1.52(b)(4). A new abstract of the disclosure is required and must be presented on a separate sheet, apart from any other text.

Applicant is reminded that the abstract should be limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited.

Correction is required. See MPEP § 608.01(b).

Specification

11. The disclosure is objected to because of the following informalities:

a. Although the present application appears to be in sequence compliance, the disclosure contains sequences that are encompassed by the

definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2) and require sequence identifiers (i.e., SEQ ID numbers). For example, see Figures 1-3 and 7-10. "It should be noted, though, that when a sequence is presented in a drawing, regardless of the format or the manner of presentation of that sequence in the drawing, the sequence must still be included in the Sequence Listing and the sequence identifier ("SEQ ID NO:X") must be used, either in the drawing or in the Brief Description of the Drawings. See MPEP 2422.02.

b. The Brief Description of the Drawings for Figure 10 (specification at page 10) is objected to because it does not describe parts (A) and (B) as shown in Figure 10.

c. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. Consider the following title: "FRAMEWORK-PATCHED IMMUNOGLOBULINS".

d. The use of the trademark Rituxan® has been noted in this application (e.g., pg 11, line 23 of the specification). It should be capitalized wherever it appears and be accompanied by the generic terminology. Applicant's cooperation is requested in reviewing the entire disclosure for additional trademarks that require correction.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner, which might adversely affect their validity as trademarks.

Appropriate correction is required.

12. Claims 41-45 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claim 45 is indefinite in the recitation "derived" because the exact meaning of the term is not known. The term "derived" is not defined by the claim; the specification does not provide a standard for ascertaining the direction, requisite degree or endpoint of the derivatized amino acids or the derivatized framework region. It is not clear whether the "derived" amino acids and framework region from a different source of the re-engineered or framework-patched antibody are formed by chemical derivatization, substitution, deletion, insertion, attachment of a detectable marker, therapeutic molecule, or some other molecule. In the absence of a single defined art recognized meaning for the term and lacking a definition of the term in the specification, one of skill in the art could not determine the metes and bounds of the claims.

b. Claim 45 is indefinite in the recitation "wherein the parent amino acids replace corresponding amino acids in the patching FR, wherein the patching FR is the FR derived from a different source used for patching, or that replaces the original FR of, the parent immunoglobulin." It is ambiguous what amino acids are being patched or replaced and in which antibody they are being patched or replaced. For example, assume that the "parent" antibody is a mouse antibody

and the "patching" antibody is a human antibody, then following the claim language the parent amino acids (mouse amino acids) replace the corresponding amino acids in the patching FR (human FR), however, the claim also recites wherein the patching FR (human FR) is used for patching or replacing the original FR of the parent or mouse antibody. Thus, it is not clear which sequence is being patched and which sequence is used for the patching. Are the parent amino acid replacements after patching with the human FR amino acids (i.e., back mutations) and what are the criteria for their selection?

c. Claims 41-44 are indefinite in the recitation "prior experience". The term "prior experience" is a relative term, which renders the claim indefinite. A determination of which FR amino acids to be patched in the claimed method is a function of the sequence or structure of the variable regions of the parent antibody compared to the antibody of a different species and any such "prior experience" with a particular antibody or CDR-FR sequence would not necessarily extrapolate to a structurally different antibody, for example. The term "prior experience" implies that the one skilled in the art has a working knowledge of the effect of changing particular amino acid residues of a given antibody on the binding affinity or on possible interactions of these residues with other Fv residues, however, the claims are not drawn to any particular antibody antibody. Thus, it is not clear what "prior experience" is being relied upon and the "prior experience" could mean experience analyzing amino acid sequences, antibody sequences, structural conservation, CDRs, antigen-binding sites, canonical

structures, solvent accessible surface area or some other "prior experience". Therefore, the term "prior experience" recited in the claims does not provide sufficient clarity and precision such that one of ordinary skill in the art could readily ascertain the metes and bounds of the claims.

13. Claims 40-49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Queen et al (US Patent 5,693,762, issues 12/2/1997, IDS filed 6/27/2001) in view of Cohen et al (U.S. Patent 5,908,925, issued 6/1/1999) and Benhar et al (Proc. Natl. Acad. Sci. USA, 91(25):12051-12055, December 6, 1994).

The claims are drawn to a re-engineered or framework (FR)-patched (i.e., humanized antibody) containing (a) heavy or/and light chain variable domain sequence(s) from a parent antibody wherein at least one of the compartmentalized or individual FR sequences, defined as FR1, FR2, FR3 and FR4 are replaced or patched with the corresponding compartmentalized or individual FR sequences from the heavy or/and light chain variable domain sequence(s) of a different species wherein the compartmentalized FR sequences are from at least two different immunoglobulin chains from the same species or from different species and wherein the re-engineered antibody binds antigen with an affinity of at least 3-fold within that of the parent antibody with the proviso that not all of the replaced or patched FR1, FR2 and FR3 of the re-engineered heavy and light chains are from the same framework of a single immunoglobulin heavy and light chain, respectively, and the re-engineered or FR-patched antibody specifically binds to an antigen with an affinity of between 10^7 M^{-1} and 10^{11} M^{-1} or

between 10^8 M^{-1} and 10^{10} M^{-1} and the re-engineered or FR-patched antibody is substantially pure or present in a pharmaceutical composition comprising in a pharmaceutically acceptable carrier. Further, the particular FR chosen for patching or replacing each corresponding FR in the parent antibody exhibits at least 60% homology to the corresponding parent FR, exhibits identical sequence homology to the corresponding parent FR at the three or four amino acids immediately adjacent to the flanking CDRs or contains conservatively similar amino acids at the three or four amino acids immediately adjacent to the flanking CDRs and contains identical or conservatively similar amino acids to the corresponding parent FR at positions known to be close to or have interactions with the CDRs/antigen binding site as evaluated by computer, crystal structure, published information or prior experience and wherein the patching FR (i.e., the FR from a different source) contains some amino acids that are identical to the amino acids in the corresponding parent FR (interpretation of claim 45).

Queen et al teach a humanized or re-engineered antibody containing heavy and light chain variable regions from a donor antibody (i.e., non-human antibody or "parental antibody") wherein the FR region sequences (i.e., all of FR1-FR4) are from a different species (i.e., human FR regions) and wherein the humanized antibody retains the antigen specificity and affinity within about 2-fold (preferably) of that of the parental antibody and wherein the affinity is from about 10^8 M^{-1} or higher (i.e., between 10^7 M^{-1} and 10^{11} M^{-1} or 10^8 M^{-1} and 10^{10} M^{-1}) and the selection of the most homologous FR region minimizes the number of amino acid changes in going from the donor or parental antibody to the humanized

antibody and reduces the risk of changing an amino acid near the CDRs that distorts their conformation and may reduce affinity. Queen et al also teach that amino acids immediately adjacent to the CDRs are likely to interact with the CDRs or make direct contact with the antigen and it is desirable to select these amino acids from the parental antibody to keep all the antigen contacts that provide antigen affinity and Queen teach the use of donor or parental amino acids at positions that are close to or interact with the CDRs based on a 3-dimensional model (i.e., crystal structure) (see entire document, particularly column 3, lines 27-43, column 10, lines 57-64, column 12, lines 37-63, column 13, lines 14-27 and column 14, lines 25-50). Further, Queen et al teach substantially pure humanized antibodies and pharmaceutical compositions comprising a humanized antibody and an acceptable carrier (i.e., pharmaceutically acceptable carrier), which were known or apparent to those skilled in the art (see column 18, line 60 to column 19, line 2 and column 23, line 55 to column 24, line 21). Queen et al teach that humanized antibodies are less immunogenic in humans compared to mouse antibodies and thus, better suited for human therapy (see column 10, lines 54-60, 64-67 and column 16, lines 14-19, for examples). Queen et al do not specifically teach a humanized or re-engineered antibody comprising FR's that are from different heavy chain variable regions and from different light chain variable regions, wherein each FR region exhibits at least 60% homology to the corresponding parent FR and exhibits identical sequence homology or conservatively similar amino acids at the three or

at the four amino acids immediately adjacent to the CDRs. These deficiencies are made up for in the teachings of Cohen et al and Benhar et al.

Cohen et al teach a humanized antibody wherein each FR is used to search for the most homologous human sequences for each non-human FR wherein the sequence identity was higher (i.e., 70-100%) for individual (i.e., compartmentalized) FR's as compared to complete VH and VL sequences due to the inclusion of the CDRs (see column 5, lines 30-41). Cohen et al also teach that it is desirable to maintain at least the major amino acid differences (size and charge) (i.e., conservatively similar) within 4 amino acids of the CDRs since these residues can have functional importance (see column 5, lines 58-63).

Benhar et al teach a rapid method of producing a humanized antibody by FR-patching wherein the parental (i.e., non-human) FR residues that differ from human FR residues are mutated to human residues to encode a human framework and the 4 amino acids immediately adjacent to the CDRs are identical to the parental FR residues (see entire document, particularly page 12053, left column and Figure 3).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to have produced a humanized (re-engineered or FR-patched) antibody wherein each individual parental FR is replaced or patched with the most homologous FR's from different sources (i.e., not from the same heavy chain variable region and not from the same light chain variable region), exhibits identical sequence homology or conservatively similar amino acids to the corresponding parent FR at the four amino acids immediately

adjacent to the CDRs and contains identical amino acids to the corresponding parent FR at positions that are close to or interact with the CDRs as evaluated by crystal structure and wherein the re-engineered or FR-patched antibody has an affinity within 2-fold of that of the parent antibody, wherein the affinity is from about 10^8 M^{-1} or higher and the humanized antibody is substantially pure or combined with a pharmaceutically acceptable carrier in a pharmaceutical composition for the treatment of a human disorder.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success at the time the invention was made to have produced a humanized (re-engineered or FR-patched) antibody wherein each individual parental FR is replaced or patched with the most homologous FR's from different sources (i.e., not from the same heavy chain variable region and not from the same light chain variable region), exhibits identical sequence homology or conservatively similar amino acids to the corresponding parent FR at the four amino acids immediately adjacent to the CDRs and contains identical amino acids to the corresponding parent FR at positions that are close to or interact with the CDRs as evaluated by crystal structure and wherein the re-engineered or FR-patched antibody has an affinity within 2-fold of that of the parent antibody, wherein the affinity is from about 10^8 M^{-1} or higher and the humanized antibody is substantially pure or combined with a pharmaceutically acceptable carrier in a pharmaceutical composition for the treatment of a human disorder in view of Queen et al and Cohen et al and Benhar et al because Queen et al teach a re-engineered or humanized antibody containing heavy and light

chain variable regions from a parental antibody wherein the FR region sequences (i.e., all of FR1-FR4) are selected from human sequences wherein the humanized antibody retains the antigen specificity and affinity within about 2-fold of that of the parental antibody and wherein the affinity is from about 10^8 M^{-1} or higher and Queen uses the most homologous human FR region to minimize the number of amino acid changes in going from the parental antibody to the humanized antibody, which also reduces the risk of changing an amino acid near the CDRs that could distort their conformation and according to Queen amino acids immediately adjacent to the CDRs as well as amino acids determined to be close to or interacting with the CDRs based on a 3-dimensional model (i.e., crystal structure) should be maintained in the humanized antibody (i.e., identical amino acid identity to the corresponding parent FR positions) since these amino acids are likely to interact with the CDRs or make direct contact with the antigen and Cohen et al teach a humanized antibody wherein each FR is used to search for the most homologous human sequences for each non-human FR wherein the sequence identity was higher for individual frameworks as compared to complete VH and VL sequences due to the presence of the CDRs and Cohen indicates desirability in maintaining at least the major amino acid differences (size and charge) within 4 amino acids of the CDRs since these residues can have functional importance and Benhar et al teach a rapid method of producing a humanized antibody by FR-patching wherein the parental FR residues that differ from human FR residues are mutated to human residues to encode a human FR and the 4 amino acids immediately adjacent to the CDRs are identical to the

parental FR residues. Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to modify the teachings of Queen et al to produce a humanized antibody wherein the most homologous individual human FR's (i.e., FR1, FR2, FR3 and FR4) are selected from different human variable regions as taught by Cohen et al to minimize the number of amino acid changes in going from the parental antibody to the humanized antibody in the FR-exchange method of Benhar et al and which also reduces the risk of changing an amino acid near the CDRs that distorts their conformation and reduces affinity. Further, one of ordinary skill in the art at the time the invention was made would have been motivated to avoid distortion of the CDRs and reduced affinity in the humanized antibody by selecting individual human FR's that contain identical or at least conservatively similar amino acids at the four amino acids immediately adjacent to the CDRs as taught by Cohen and Benhar as well as select individual human FR's that contain identical amino acids to the corresponding parental FR's at positions known to be close to or interact with the CDRs based on a 3-dimensional model as taught by Queen. Thus, there would be an advantage to selecting individual or compartmentalized FR's (i.e., FR1, FR2, FR3 and FR4) rather than selecting FR regions based on homology of complete variable regions (i.e., VH and VL), which reduces amino acid identity due to the inclusion of the CDRs as taught by Cohen and increased homology of the individual FR's minimizes the number of mutations that are required in the FR-patching method of Benhar for producing a humanized antibody and the advantages of maintaining sequence identity at the four amino

acids immediately adjacent to the CDRs and at FR positions that are close to or interact with the CDRs as determined by a 3-dimensional model are made explicit in the teachings of Queen, which indicate that amino acid changes at these positions may distort the CDRs and reduce affinity in the humanized antibody. Thus, it would have been *prima facie* obvious to one skilled in the art at the time the invention was made to have produced a humanized (re-engineered or FR-patched) antibody wherein each individual parental FR is replaced or patched with the most homologous FR's from different sources (i.e., not from the same heavy chain variable region and not from the same light chain variable region), exhibits identical sequence homology or conservatively similar amino acids to the corresponding parent FR at the four amino acids immediately adjacent to the CDRs and contains identical amino acids to the corresponding parent FR at positions that are close to or interact with the CDRs as evaluated by crystal structure and wherein the re-engineered or FR-patched antibody has an affinity within 2-fold of that of the parent antibody, wherein the affinity is from about 10^8 M^{-1} or higher and the humanized antibody is substantially pure or combined with a pharmaceutically acceptable carrier in a pharmaceutical composition for the treatment of a human disorder in view of Queen et al and Cohen et al and Benhar et al.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Double Patenting

14. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

15. Claims 40-49 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-13 of copending Application No. 10/482,759. Although the conflicting claims are not identical, they are not patentably distinct from each other.

Instant claims 40-49 have been described supra. For this rejection, claim 45 is interpreted as drawn to the re-engineered or FR-patched antibody in which the particular FR chosen for patching each corresponding FR in the parent immunoglobulin comprises re-introduced amino acids from the parent immunoglobulin framework outside the Kabat and Chlothia CDRs wherein the

parent (i.e., re-introduced) amino acids replace corresponding amino acids in the patching FR, wherein the patching FR is the FR obtained from a different source that replaces the original FR of the parent immunoglobulin.

Claims 1-13 of copending Application No. 10/482,759 are also drawn to a re-engineered or framework (FR)-patched immunolgobulin containing heavy and/or light chain variable region sequence(s) from a parent antibody wherein at least one of the compartmentalized framework sequences, defined as FR1, FR2, FR3 and FR4 are replaced or patched with the corresponding FR sequences from the heavy and light chain variable domain sequences of a different species wherein the compartmentalized FR sequences are from at least two different sources immunoglobulin chains from different immunoglobulin chains from the same species or from different species and wherein the re-engineered or FR-patched antibody binds antigen with an affinity within 3-fold of that of the parent antibody, and the re-engineered or FR-patched antibody specifically binds to an antigen with an affinity of between 10^7 M^{-1} and 10^{11} M^{-1} or between 10^8 M^{-1} and 10^{10} M^{-1} and the re-engineered or FR-patched antibody is substantially pure or present in a pharmaceutical composition comprising in a pharmaceutically acceptable carrier. Further, the particular FR chosen for patching or replacing each corresponding FR in the parent antibody exhibits the highest degree of homology, or at least 60% homology to the corresponding parent FR, exhibits identical sequence homology to the corresponding parent FR at the three or four amino acids immediately adjacent to the flanking CDRs or contains conservatively similar amino acids at the three or four amino acids immediately

adjacent to the flanking CDRs and contains identical or conservatively similar amino acids to the corresponding parent FR at positions known to be close to or have interactions with the CDRs/antigen binding site as evaluated by computer, crystal structure, published information or prior experience. Thus, instant claims 40-44 and 46-49 are obvious variants claims 1-5 and 10-13 of copending Application No. 10/482,759 because FR sequences from at least two different sources of immunoglobulin chains from different immunoglobulin chains.from the same species or from different species encompasses FR1, FR2, FR3 and FR4 obtained from different sources of immunoglobulin chains. Further, claims 6-9 of copending Application No. 10/482,759 are drawn to the re-engineered or FR-patched antibody in which the particular FR chosen for patching each corresponding FR in the parent immunoglobulin comprises re-introduced amino acids from the parent immunoglobulin framework outside the Kabat and Chlothia CDRs wherein the back mutated (i.e., re-introduced) amino acids replace corresponding amino acids in the patching FR, wherein the patching FR is the FR obtained from a different source that replaces the original FR of the parent immunoglobulin and each of said back mutated amino acids is adjacent to a CDR in the donor immuoglobulin sequence or contains an atom within a distance of 4 Angstroms, 5 Angstroms or 6 Angstoms in the re-engineered or FR-patched immunoglobulin, is adjacent to a CDR in the donor immuoglobulin sequence or is capable of interacting with amino acids in the CDRs or is typical at its position for the species of the particular FR chosen for the patching and the replaced amino acid in the said FR is rare at its position for the species from where the FR is

derived and instant claim 45 is interpreted as drawn to the re-engineered or FR-patched antibody in which the particular FR chosen for patching each corresponding FR in the parent immunoglobulin comprises re-introduced amino acids from the parent immunoglobulin framework outside the Kabat and Chlothia CDRs wherein the parent (i.e., re-introduced) amino acids replace corresponding amino acids in the patching FR, wherein the patching FR is the FR obtained from a different source that replaces the original FR of the parent immunoglobulin. Thus, instant claim 45 is a genus upon which claims 6-9 of copending Application No. 10/482,759 read, i.e., species anticipates the genus.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

16. No claim is allowed.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Blanchard whose telephone number is (571) 272-0827. The examiner can normally be reached at Monday through Friday from 8:00 AM to 6:00 PM, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached at (571) 272-0832. The official fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the patent Application Information Retrieval (PAIR) system. Status information

for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,
David J. Blanchard
571-272-0827